

REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1-11, 17-20, and 39-46, the only claims pending and under examination in this application.

Claims 31-38 have been cancelled.

New Claims 39-46 have been added. Support for new Claim 39 can be found in the specification for example on p. 11, line 17-p. 12, line 3. Support for new Claim 40 can be found in the specification for example on p. 46, lines 3-7. Support for new Claims 41 and 42 can be found in the specification for example on p. 39, lines 14-31. Support for new Claim 43 can be found in the specification for example on p. 35, line 8-p. 36, line 2; and p. 52, lines 7-16. Support for new Claim 44 can be found in the specification for example on p. 12, lines 15-26. Support for new Claims 45 and 46 can be found in the specification for example on p. 37, lines 5-17. Accordingly, no new matter has been added.

As no new matter has been added by the above amendments, entry thereof by the Examiner is respectfully requested.

Claim Rejections - 35 U.S.C. § 102

The Applicants note that the previous rejection of Claims 2 and 3 under 35 U.S.C. § 102(e) as anticipated by Rezai (US Publication No. 2005/0065574) have been withdrawn.

Claim Rejections - 35 U.S.C. § 103

Claims 1, 4, 7, 9, 10, 17, 18 and 20 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rezai (US Publication No. 2005/0065574) in view of Verrier et al. (5,437,285).

The rejected claims are directed to a method of treating a female subject known to suffer from a fertility condition. The method includes modulating at least a portion of the autonomic nervous system of the female subject to increase the sympathetic activity/parasympathetic activity ratio so as to treat a female subject for a fertility condition. The method further includes determining the ratio of sympathetic activity to parasympathetic activity prior to the modulation and performing the modulation of a portion of the autonomic nervous system based on the determined ratio of sympathetic activity to parasympathetic activity.

In maintaining the rejection, the Examiner alleges that although Rezai does not disclose determining a ratio of sympathetic activity to parasympathetic activity, Verrier, et al., allegedly teaches that sympathetic/parasympathetic balance is one such "pattern of neuronal activity" that is used as a feedback mechanism of autonomic influence for stimulators.

The Applicants again respectfully disagree with this assertion, for reasons of record, and again argue that Rezai does not teach or suggest determining a ratio of sympathetic activity to parasympathetic activity. The addition of Verrier does not make up for this deficiency, because Verrier simply discloses a ratio of the low frequency component and the high frequency component of heart rate variability of an individual with a potentially fatal heart condition.

Furthermore, the Applicants note that as discussed in the previous response, the method in Rezai includes a simple measurement of neuronal activity. The "sensor signal" for the closed-loop feedback mechanism in Rezai is, therefore, a measurement such as synaptic potential. There is no disclosure in Rezai of determining a ratio of neuronal activity, which would require measuring sympathetic activity, measuring parasympathetic activity, and then comparing the two measured activities to determine a ratio.

Rezai is therefore silent as to determining a ratio of any kind. The ratio in Verrier is specifically limited to patients with heart conditions, and there is no indication or suggestion in the references that determining a ratio of the low frequency component and the high frequency component of heart rate variability as in heart patients would have any relevance to treating a female for a fertility condition.

The Examiner has asserted that Rezai teaches a closed-loop system to control the autonomic stimulation for treating a fertility condition, as discussed above, and that sympathetic/parasympathetic balance is one such "pattern of neuronal activity" that is used as a feedback mechanism of autonomic influence for stimulators.(Final Office Action, p. 7) . However, as argued above, the "sensor signal" for the closed-loop feedback mechanism in Rezai is simply measuring neuronal activity. There is no disclosure of determining a ratio of any kind. The Examiner has not provided any valid apparent reason why one of ordinary skill in the art would have combined a method of determining a ratio with a closed-loop feedback system where the "sensor signal" is a simple measurement of neuronal activity.

Again, the Applicants note that the Examiner cites Schuler (US 2006/0224189) (Advisory Action, p. 2) for support for a feedback mechanism of autonomic influence. Schuler discloses a "method to record, store and broadcast specific brain waveforms to modulate body organ functioning" (see title). There is no disclosure in this reference of measuring a sympathetic activity/parasympathetic activity ratio, or measuring a ratio of any kind. It is not clear to the Applicants how this reference provides support for the Examiner's argument.

In view of the above, the Applicants contend that a *prima facie* case of obviousness has not been established because the combination of Rezai and Verrier fails to teach or suggest all the claimed limitations, namely modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic

activity/parasympathetic activity ratio in a manner effective to treat a fertility condition, further comprising determining said sympathetic activity/parasympathetic activity ratio at least prior to said modulation and performing said modulation of said at least one portion of the autonomic nervous system based on the ratio. Furthermore, the Examiner has not pointed to any valid apparent reason why one of ordinary skill in the art would have combined the methods of Rezai with the ratio in Verrier. Consequently, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1, 4, 7, 9, 10, 17, 18 and 20 be withdrawn.

Claims 2 and 3 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Rezai in view of Bothe Loncar et al. (US Publication No. 2002/0188336).

As set forth above, elements of the rejected claims are directed to a method of treating a female subject known to suffer from a fertility condition. The method includes determining a sympathetic activity/parasympathetic activity ratio and modulating at least a portion of the autonomic nervous system based on the determined sympathetic activity/parasympathetic activity ratio so as to treat the female subject for the fertility condition.

As discussed above, Rezai does not disclose determining a ratio of sympathetic activity to parasympathetic activity, much less modulating at least a portion of the autonomic nervous system based on the determined sympathetic activity/parasympathetic activity ratio. Therefore, Rezai does not teach or suggest all the claim limitations. As Bothe Loncar is cited solely for its alleged disclosure of modulating the autonomic nervous system during the luteal phase of the menstrual cycle, it fails to remedy the deficiencies of Rezai.

Therefore, a *prima facie* case of obviousness has not been established because the combination of Rezai and Bothe Loncar fails to teach or suggest all the claimed limitations, namely modulating a portion of the autonomic nervous system based on the

determined sympathetic activity/parasympathetic activity ratio so as to treat a female subject for a fertility condition. The Applicants' therefore respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 2 and 3 over Rezai in view of Bothe Loncar be withdrawn.

Claims 5, 6 and 11 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rezai in view of Whitehurst et al. (USPN 6,832,114).

Claims 5, 6 and 11 depend from Claim 1. As set forth above, Claim 1 is directed to a method of modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic activity/parasympathetic activity ratio so as to treat the female subject for a fertility condition.

As described above, Rezai discloses affecting a "hypothalamic-related condition" by electrically or chemically stimulating the hypothalamus (see Abstract), and discloses a list of over 55 conditions allegedly related to the hypothalamus (page 9, Table II). However, Rezai does not disclose determining the sympathetic activity/parasympathetic activity ratio of a subject and modulating the ANS of the subject based on the determined sympathetic activity/parasympathetic activity ratio.

The addition of Whitehurst et al. does not cure the deficiency of Rezai. Whitehurst et al. disclose modulating a patient's pancreatic endocrine secretion by electrical stimulation to treat diabetes. However, Whitehurst et al. do not disclose determining the sympathetic activity/parasympathetic activity ratio of a subject and modulating at least a portion of the autonomic nervous system of the subject to increase the sympathetic activity/parasympathetic activity ratio of the subject.

Since neither Rezai nor Whitehurst et al. disclose this claim element, both references, either alone or combined, do not teach or suggest all the claim limitations of Claims 5, 6 and 11.

In view of the above, the Applicants contend that a *prima facie* case of obviousness has not been established because the combination of Rezai with Whitehurst fails to teach or suggest all the claimed limitations, namely modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic activity/parasympathetic activity ratio in manner effective to treat a female subject for a fertility condition. Consequently, the Applicants respectfully request that the the 35 U.S.C. § 103(a) rejection of Claims 5, 6, and 11 be withdrawn.

Claim 8 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rezai in view of Mann et al. (US Publication No. 2002/0055761).

Claim 8 depends from Claim 1. As set forth above, Rezai fails to teach or suggest modulating a portion of the autonomic nervous system based on the determined sympathetic activity/parasympathetic activity ratio so as to treat a female subject for a fertility condition. As Mann is cited solely for its alleged disclosure of stimulating a pelvic nerve (i.e., to treat incontinence, urgency, frequency, or pelvic pain), it fails to remedy the deficiencies of Rezai. Mann does not disclose determining the sympathetic activity/parasympathetic activity ratio of a subject and modulating the ANS of the subject based on the determined sympathetic activity/parasympathetic activity ratio.

Since neither Rezai nor Mann et al. disclose this claim element, both references, either alone or combined, do not teach or suggest all the claim limitations of Claim 8.

Therefore, a *prima facie* case of obviousness has not been established because the combination of Rezai with Mann fails to teach or suggest all the claimed limitations, namely modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic activity/parasympathetic activity ratio in manner

effective to treat a female subject for a fertility condition. The Applicants therefore respectfully request that the 35 U.S.C. § 103(a) rejection of Claim 8 be withdrawn.

Claim 19 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rezai in view of Khan et al. (US Publication No. 2002/0064501).

Claim 19 depends from Claim 1. As set forth above, elements of the rejected claims include a method of modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic activity/parasympathetic activity ratio so as to treat the female subject for a fertility condition. As described above, Rezai fails to teach or suggest modulating a portion of the autonomic nervous system based on the determined sympathetic activity/parasympathetic activity ratio so as to treat a female subject for a fertility condition.

The addition of Khan does not remedy the deficiency of Rezai. Khan discloses using an immunoregulator to treat an immune-mediated disorder, including "chronic inflammatory disease, such as diabetes type I or II, rheumatic disease, Sjogrens syndrome, multiple sclerosis, transplantation-related immune responses such as graft-versus-host-disease, post-transfusion thrombocytopenia, chronic transplant rejection, pre-eclampsia, atherosclerosis, asthma, allergy and chronic auto-immune disease, and acute inflammatory disease" (paragraph [0028]). However, Khan does not disclose determining the sympathetic activity/parasympathetic activity ratio of a subject and modulating the ANS of the subject based on the determined sympathetic activity/parasympathetic activity ratio.

Therefore, Khan does not remedy the deficiencies of Rezai. Consequently, a *prima facie* case of obviousness has not been established because the combination of Rezai and Khan fails to teach or suggest all the claimed limitations, namely modulating at least a portion of the autonomic nervous system of a female subject to increase the sympathetic activity/parasympathetic activity ratio in manner effective to treat a female

subject for a fertility condition. Consequently, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claim 19 be withdrawn.

The Applicants submit that new Claims 39-46 are patentable over the art cited by the Examiner at least for the reasons cited above.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 833-7770.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number PALO-004.

Respectfully submitted,
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